Curing Sickle cell Disease with CRISPR-Cas9 genome editing

Grant Award Details

Curing Sickle cell Disease with CRISPR-Cas9 genome editing

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-09292-B

Project Objective: Conduct a pre-IND meeting and prepare protocol for CRISPR/Cas9 gene edited autologous HSC therapy to cure sickle cell disease

Investigator:

Name:	Mark Walters
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: Blood Disorders, Sickle Cell Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: $25,000

Status: Pre-Active

Grant Application Details

Application Title: Curing Sickle cell Disease with CRISPR-Cas9 genome editing

Public Abstract:

Translational Candidate

The principal objective of this program is to bring a Cas9-based gene editing cure for sickle cell disease to the pre-IND stage of development.

Area of Impact

The principal barriers to transplant for SCD are lack of a donor and the toxicity of transplant, which can be overcome by the Cas9-based approach

Mechanism of Action

Ex vivo editing of autologous stem cells would be followed by re-implantation of edited cells, bypassing donor requirements and eliminating risks of graft-versus-host disease and rejection. Because sickle RBCs have a markedly reduced lifespan, low level sickle gene correction would be predicted to generate a clinical benefit by virtue of enrichment of the longer-lived corrected RBCs in circulation. After conventional transplant, clinical benefit with as few as 2-5% donor HSCs has been observed.

Unmet Medical Need

Fewer than 1% of individuals with sickle cell disease pursue an allogeneic bone marrow transplant cure today, principally because most affected persons lack a suitable donor. This proposal could make a cure universally available because it corrects the sickle mutation in a persons' own stem cells.

Project Objective

conduct a pre-IND meeting and prepare a protocol

Major Proposed Activities

- Test Optimal Editing Reagents in stem cells from subjects with sickle cell disease and show correction in >2% sickle stem cells
- Translate optimal method for gene editing with GMP-comparable reagents and processes for cell processing and cryopreservation.
- Ramp-up testing of reagents to manufacture a demonstration clinical-scale lot of the gene-corrected CD34+ cell product that meets all release criteria

Statement of Benefit to California:

Sickle cell disease (SCD) affects over 6000 primarily African-Americans in California. A survival of <40 years of age was observed in a large cohort of California patients. The estimated lifetime cost of care is $9 million per person. This project aims to improve SCD therapy by preparing for a clinical trial that might cure SCD after giving back sickle gene-corrected hematopoietic stem cells to a person with SCD. If successful, this would be a universal life-saving and cost-saving therapy.
